Bmi-1 is a crucial regulator of prostate stem cell self-renewal and malignant transformation.

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Authors: Rita U Lukacs, Sanaz Memarzadeh, Hong Wu, Owen N Witte

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Public Summary:
The Polycomb group transcriptional repressor Bmi-1 is often upregulated in prostate cancer, but its functional roles in prostate stem cell maintenance and prostate cancer are unclear. Loss- and gain-of-function analysis in a prostate sphere assay indicates that Bmi-1 expression is required for self-renewal activity and maintenance of p63(+) stem cells. Loss of Bmi-1 blocks the self-renewal activity induced by heightened beta-catenin signaling, suggesting that Bmi-1 is required for full activity of another self-renewal pathway. In vivo, Bmi-1 expression is necessary for normal prostate tubule regeneration. Altered self-renewal and proliferation through Bmi-1 modulation diminishes the susceptibility of prostate cells to transformation. In an in vivo prostate regeneration system, Bmi-1 inhibition protects prostate cells from FGF10-driven hyperplasia and slows the growth of aggressive Pten-deletion-induced prostate cancer. We conclude that Bmi-1 is a crucial regulator of self-renewal in adult prostate cells and plays important roles in prostate cancer initiation and progression.

Scientific Abstract:
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